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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,997	06/20/2003	James P. Allison	A-71608/TAL/DHR (465174-4	5773

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,997	ALLISON ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1087* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1087* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1 – 87 are pending.

2. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

3. For examination purposes the following is noted:

The instant claims contain recitations of multiple "agonists" and "antagonists." These molecules are patentably distinct because their structures, physicochemical properties and/or mode of action are different, and they do not share a common structure that is disclosed to be essential for common utility. Therefore, the restriction has been set forth for each as separate groups, irrespective of the format of the claims.

The instant claims contain recitations of "modulating," thus encompassing methods of upregulating as well as downregulating immune response. These methods are mutually exclusive in that they reach opposing endpoints, and in that they employ structurally distinct agents to accomplish these mutually exclusive endpoints. Consequently, the restriction has been set forth for methods relating to downregulation, and for methods relating to upregulation, as separate groups, irrespective of the format of the claims.

The instant claims contain recitations of multiple amino acid and nucleic acid sequences. These molecules are patentably distinct because their structures, physicochemical properties and/or mode of action are different, and they do not share a common structure that is disclosed to be essential for common utility. Therefore, the restriction has been set forth for each as separate groups, irrespective of the format of the claims.

Restriction Requirement

4. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1 – 5, 9 – 10, 17 – 23, 27 – 28, 50 – 52, and 56 – 57, drawn to a method for increasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an antagonist of BTLA signaling, wherein the antagonist is an anti-BTLA antibody, classified in Class 424, subclass 130.1.

II. Claims 1 – 4, 6 – 7, 9 – 10, 17 – 22, 24 – 25, 27 – 28, 50 – 51, 53 - 54 and 56 – 57, drawn to a method for increasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an antagonist of BTLA signaling, wherein the antagonist is a soluble BTLA protein or fusion protein, classified in Class 514, subclass 12.

III. Claims 1 – 4, 8 – 10, 17 – 22, 26 – 28, 50 – 5, and 55 – 57, drawn to a method for increasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an antagonist of BTLA signaling, wherein the antagonist is an anti-B7x antibody, classified in Class 424, subclass 130.1.

IV. Claims 1 – 4, 9 – 10, 17 – 22, 27 – 28, 50 – 51, and 56 – 57, drawn to a method for increasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an antagonist of BTLA signaling, wherein the antagonist is a small molecule, classified in Class 514, subclass 1.

V. Claims 1 – 4, 10, 17 – 22, 28, 50 – 51, and 57, drawn to a method for increasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an

antagonist of BTLA signaling, wherein the antagonist is a BTLA antisense oligonucleotide, classified in Class 514, subclass 44.

VI. Claims 1 – 4, 10, 17 – 22, 28, 50 – 51, and 57, drawn to a method for increasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an antagonist of BTLA signaling; wherein the antagonist is a B7x antisense oligonucleotide, classified in Class 514, subclass 44.

VII. Claims 1, 11 – 20, 29 – 34, and 58 – 63, drawn to a method for decreasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an agonist of BTLA signaling, wherein the agonist is a soluble B7x protein or fusion protein, classified in Class 530, subclass 350.

VIII. Claims 1, 11 – 13, 16 – 20, 29 – 31, 34, 58 – 60, and 63, drawn to a method for decreasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an agonist of BTLA signaling, wherein the agonist is a small molecule, classified in Class 514, subclass 1.

IX. Claims 1, 11 – 13, 16 – 20, 29 – 31, 34, 58 – 60, and 63, drawn to a method for decreasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an agonist of BTLA signaling, wherein the agonist is an expression vector comprising a BTLA-encoding polynucleotide, classified in Class 514, subclass 44.

X. Claims 1, 11 – 13, 16 – 20, 29 – 31, 34, 58 – 60, and 63, drawn to a method for decreasing lymphocyte activity by contacting a BTLA-positive lymphocyte with an agonist of BTLA signaling, wherein the agonist is an expression vector comprising a B7x-encoding polynucleotide, classified in Class 514, subclass 44.

XI. Claims 35 – 38 and 42 – 43, drawn to a bioactive agent comprising an anti-BTLA antibody, classified in Class 424, subclass 130.1.

XII. Claims 35 – 37, 39 – 40, and 42 – 43, drawn to a bioactive agent comprising a soluble BTLA protein or fusion protein, classified in Class 514, subclass 12.

XIII. Claims 35 – 37 and 41 – 43, drawn to a bioactive agent comprising an anti-B7x antibody, classified in Class 424, subclass 130.1.

XIV. Claims 35 – 37 and 42 – 43, drawn to a bioactive agent comprising a small molecular weight inhibitor of the interaction between BTLA and B7x, BTLA expression, or BTLA-mediated signaling, classified in Class 514, subclass 1.

XV. Claims 35 – 37 and 43, drawn to a bioactive agent comprising BTLA antisense oligonucleotides, classified in Class 514, subclass 44.

XVI. Claims 35 – 37 and 43, drawn to a bioactive agent comprising BTLA small RNA inhibitors, classified in Class 514, subclass 44.

XVII. Claims 44 – 49, drawn to a bioactive agent comprising a B7x protein or fusion protein, classified in Class 514, subclass 12.

XVIII. Claims 44 – 46 and 49, drawn to a bioactive agent comprising a small molecular weight enhancer of BTLA-mediated signaling, classified in Class 514, subclass 1.

XIX. Claims 44 – 46 and 49, drawn to a bioactive agent comprising expression vectors comprising BTLA nucleic acids, classified in Class 514, subclass 44.

XX. Claims 44 – 46 and 49, drawn to a bioactive agent comprising expression vectors comprising B7x nucleic acids, classified in Class 514, subclass 44.

XXI. Claims 64 – 78, drawn to a recombinant BTLA nucleic acid of SEQ ID NO:7, or encoding a polypeptide of SEQ ID NO:8; as well as vectors, host cells and methods of producing the polypeptide, classified in Class 536, subclass 23.5, and Class 435, subclasses 320.1, 252.3, 455 and 69.1.

XXII. Claims 64 – 78, drawn to a recombinant BTLA nucleic acid of SEQ ID NO:9, or encoding a polypeptide of SEQ ID NO:10; as well as vectors, host cells and methods of producing the polypeptide, classified in Class 536, subclass 23.5, and Class 435, subclasses 320.1, 252.3, 455 and 69.1.

XXIII. Claims 79 – 87, drawn to a BTLA protein of SEQ ID NO:8, or encoded by a polypeptide of SEQ ID NO:7, classified in Class 530, subclass 350.

XXIV. Claims 79 – 87, drawn to a BTLA protein of SEQ ID NO:10, or encoded by a polypeptide of SEQ ID NO:9, classified in Class 530, subclass 350.

5. Groups I – X are different methods. The methods differ with respect to one or more of ingredients, method steps, and/or endpoints; therefore, each method is patentably distinct. Furthermore, the distinct ingredients, method steps, and/or endpoints require separate and distinct searches. As such, it would be burdensome to search these Inventions together.

Groups XI – XXIV are different products. The products are patentably distinct because their structures, physicochemical properties and/or mode of action are different, and they do not share a common structure that is disclosed to be essential for

common utility. Furthermore, they require non-coextensive searches in the scientific literature. Therefore, each product is patentably distinct, and searching of these Inventions would impose an undue burden.

Groups (XI – XXIV) and (I – X) are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products of Groups I – X can be used for diagnostic purposes, in addition to the methods recited.

6. These inventions are distinct for the reasons given above. In addition, they have acquired a separate status in the art as shown by different classification and/or recognized divergent subject matter. Further, even though in some cases the classification is shared, a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Moreover, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention. Therefore restriction for examination purposes as indicated is proper.

Species Election

7. This application contains claims directed to the following patentably distinct Species of the claimed Inventions I – X, wherein the lymphocyte is:

A. T lymphocyte, or

B. B lymphocyte.

These species are distinct because their structures, physicochemical properties and mode of action are different, and they do not share a common structure that is disclosed to be essential for common utility. Furthermore, the examination of these species would require different searches in the scientific literature. As such, it would be burdensome to search these Species together.

Applicant is required under 35 USC 121 to elect a single disclosed species to which the claims would be restricted if no generic claim is finally held to be allowable.

8. This application contains claims directed to the following patentably distinct Species of the claimed Inventions I – X, wherein the antigen is:

A. a pathogen antigen,

B. a vaccine antigen, or

C. a tumor associated antigen.

These species are distinct because their structures, physicochemical properties and mode of action are different, and they do not share a common structure that is disclosed to be essential for common utility. Furthermore, the examination of these species would require different searches in the scientific literature. As such, it would be burdensome to search these Species together.

Applicant is required under 35 USC 121 to elect a single disclosed species to which the claims would be restricted if no generic claim is finally held to be allowable.

9. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument

that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. M.P.E.P. § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

10. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. *Process claims that depend from or otherwise include all the limitations of the patentable product* will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to

be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. *Failure to do so may result in a loss of the right to rejoinder.*

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

11. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

12. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

November 1, 2005

PHILLIP GAMBEL, PH.D
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11/1/05